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17. (Twice Amended) The primer according to claim 9, wherein the marker or the moiety bound to a solid-phase carrier is a biotin residue, a 2,4-dinitrophenyl group or a digoxigenin residue.

18. (Twice Amended) The primer according to claim 10, wherein the marker or the moiety bound to a solid-phase carrier is a biotin residue, a 2,4-dinitrophenyl group or a digoxigenin residue.--

REMARKS

The claims are 1-25 with claims 19-25 being nonelected. Applicants affirm the provisional election of Group 1, claims 1-18 and request that upon indication of allowability for Group I, that Group II be rejoined with appropriate opportunity being provided for any amendment to Group II as required. Claims 1-18 have been amended to resolve informalities under Rule 112, second paragraph and reconsideration of the claims is expressly requested.

The specification has been amended to identify nucleotide sequences by appropriated SEQ ID NOS. on pages 54 and 56, as requested.

The Examiner had objected to claims 2-18 as being of improper dependent form since they were directed to modifications that were not apparently encompassed by claim 1. Claim 1 has now been amended to encompass the desired complementary base sequences, mutations and complements of said mutations, such that claims 2-18 are now properly dependent thereon. Withdrawal of the objection is respectfully requested.

Claims 1-18 were rejected under Rule 112, second paragraph, as being indefinite. Applicants have now amended claims 1-18, as required in order to address each of the concerns raised by the Examiner. The recitation in claim 2 as to a partial sequence refers to a portion of a nucleic acid according to claim 1.

Claim 7 has been amended to provide for the presence of two different nucleic acid fragments.

With regard to claims 10-13, the Examiner had stated it was unclear as to what "into a 5' -terminal side" was intended to mean. That objection is respectfully traversed. A nucleotide sequence is generally described from the 5'-terminal side (or the left side) to the 3-terminal side (right side) direction. This is a well known technique for identifying nucleotide sequences employed by those of ordinary skill in the art.

Withdrawal of the objections under Rule 112, second paragraph, is respectfully requested.

Claims 1-13 were rejected as anticipated by Engel '779, Brennan '796 and Huisman. Claims 1-13 were rejected as obvious over Huisman in view of Solainman and Dieffenbach. Claims 1-18 were rejected as obvious over Huisman in view of Doi '805. The grounds of rejection are respectfully traversed.

Prior to addressing the grounds of rejection applicants wish to briefly review certain key features and advantages of the present claimed invention.

As disclosed on specification page 34, line 26, page 44, line 7, page 47, line 10 and page 51, line 7 an annealing (or hybridization) is carried out at a temperature of

55°C in the procedure for detecting a partial base sequence of a PHA synthethase gene by PCR method using as a template a gene DNA of a microorganism synthesizing PHA. The step for separating a double-stranded nucleic acid is typically conducted at 95°C for 20 seconds; the step of hybridization is typically conducted at 55°C for 30 seconds and the step for synthesizing a chain from the annealed portion is typically conducted at 72°C for 60 seconds.

The nucleic acid chains of the amplified products were detected according to the following procedure. For the PHA synthesizing microorganisms, one clear band was observed as described on specification page 35, lines 10-14 and at page 44, lines 19-23. In addition, significant absorption could be observed as compared with the background as disclosed on specification page 48, lines 21-24 and page 52, lines 14-17. The hybridization as performed at 55°C generally causes a mismatch from 0 to about 10 bases.

With regard to the cited prior art, the base sequences disclosed in the cited references are quite different from the base sequences of SEQ ID NOS. 1-9 of claim 1. The Examiner admits that the primary references merely disclose only trivial sequences in any of the nucleic acids claimed. Clearly, none of the references teaches nucleic acids consisting of SEQ ID NOS. 1-9, complementary base sequences of them or mutations or complementary base sequences of said mutations capable of hybridizing at 55°C with SEQ ID NOS. 1-9.

Wherefore, none of the references, whether considered alone or in combination, discloses or suggests the present claimed invention nor renders it unpatentable.

Accordingly, it is respectfully requested that the claims be allowed and that the case be passed to issue.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE TO SPECIFICATION

The paragraph beginning at page 53, line 27 and ending at page 54, line 10 has been amended with the following replacement paragraph.

--After 100 ng of a biotin-labeled oligonucleotide probe (SEQ ID NO: 13):

5' -GGCGAAAACAAGGTCAACGCCCTGACC-Biotin-3',

prepared in example 3 per 3 ml of the above prehybridization solution as a hybridization solution was added to the nylon membrane after thermal denaturation, hybridization was performed using 3 ml of this solution at 60°C for 2 hr. Thereafter, the nylon membrane was taken from the vinyl bag and washed 3 times with 6xSSC and 0.5 SDS solution at 60°C for each 5 min.--

The paragraph at page 56, lines 8-20 has been amended with the following replacement paragraph.

--The probe in which FITC (Fluorescein isothiocyanate)-labeled streptoavidin was coupled beforehand with biotin-labeled oligonucleotide probe (SEQ ID NO: 13):

5' -GGCGAAAACAAGGTCAACGCCCTGACC-Biotin-3',

prepared in example 3, was used. A solution of 30 μl in which this FITC-labeled probe in concentration of 5 ng/μl was added to the hybridization solution (0.1 M Tris-C1 buffer (pH 8.0), 0.75M NaC1, 5 mM EDTA, 10% dextran sulfate, 0.2% BSA (Bovine Serum Albumin) and 0.01% polyadenylic acid) was dropped onto a slide glass. The slide glass was placed in an airtight container and the reaction was carried out at 45°C for 1 hr in a shading state.--

VERSION WITH MARKINGS TO SHOW CHANGES MADE TO CLAIMS

--1. (Amended) [A] An isolated nucleic acid [fragment] consisting of (a) a member selected from [any of a based sequence shown in] the group consisting of SEQ ID NOS. [1-9] 1-8 and 9, (b) complementary base sequences of (a) [sequence thereof], (c) a mutation of (a) or (b) which is a [or] modified [sequence subjected to a mutation based on these sequences] sequence capable of hybridizing at 55°C with SEQ ID NOS. 1-8 and 9 and (d) complementary base sequences of said modified sequences (c).

2. (Amended) A nucleic acid fragment that can be utilized as a primer or probe comprising the nucleic acid [fragment] according to claim 1, or a nucleic acid fragment comprising a partial sequence in a base sequence [thereof] of the nucleic acid of claim 1.

3. (Amended) The isolated nucleic acid [fragment] according to claim 1, wherein [a] the mutation [based on a base sequence shown in SEQ ID NOS: 1 to 9 or a complementary base sequence thereof] is partial deletion of the base sequence, addition of an extra base or base sequence, or substitution of bases or partial sequence in the base sequence with other base or base sequence, or a combination thereof.

4. (Amended) The nucleic acid fragment according to claim 2, wherein [a] the mutation [based on a base sequence shown in SEQ ID NOS: 1 to 9 or a complementary base sequence thereof] is partial deletion of the base sequence, addition of an extra base or base sequence, or substitution of bases or partial sequence in the base sequence with other base or base sequence, or a combination thereof.

5. (Amended) A primer comprising a nucleic acid fragment that can be utilized as a primer according to any one of claims 2, 3 or 4, in which, as an additional modification, a marker [bound onto a molecule of] is attached to said nucleic acid fragment and/or a moiety [capable of binding] attached to a solid-phase carrier [may be introduced] is bound to said nucleic acid fragment.

6. (Amended) A probe comprising a nucleic acid fragment that can be utilized as a probe according to any one of claims 2, 3 or 4, in which, as an additional modification, a marker [bound onto a molecule of] is attached to said nucleic acid fragment and/or a moiety [capable of binding] attached to a solid-phase carrier is bound to said nucleic acid fragment [may be introduced].

7. (Amended) A primer comprising a combination of two [kinds] different [of] nucleic acid fragments with a substantial difference in their base sequences, wherein at least one of said two [kinds of] different nucleic acid fragments is a nucleic acid fragment for a primer according to claim 5, and a marker, and/or a moiety [capable of binding] attached to a solid-phase carrier [may be introduced into], bound to each molecule of said two nucleic acid fragments.

9. (Twice Amended) The primer according to claim 7, wherein the base sequence of said at least one of said two [kinds of] different nucleic acid fragments is a modified base sequence subjected to a mutation, comprising partial deletion of the base sequence, addition of an extra base or base sequence, or substitution of a base or partial sequence in the base sequence with other base or base sequence, or a combination thereof, based on a base sequence shown in SEQ ID NO: 1 to 9 or complementary base sequence thereof.

10. (Twice Amended) The primer according to claim 5, wherein said primer comprises at least one kind of nucleic acid fragment subjected to an additional modification, and the additional modification in one kind of said nucleic acid fragment is [introduction of] a marker or a moiety [capable of binding] bound to a solid-phase carrier, wherein said marker or moiety is additionally bound to a [into a] 5'-terminal side of the nucleic acid fragment.

11. (Twice Amended) The probe according to claim 6, wherein said probe comprises at least one kind of nucleic acid fragment subjected to an additional modification, and the additional modification in one kind of said nucleic acid fragment is [introduction of] a marker or a moiety [capable of binding] bound to a solid-phase carrier, wherein said marker or moiety is additionally bound to [into] a 5'-terminal side of the nucleic acid fragment.

12. (Twice Amended) The primer according to claim 7, wherein said primer comprises at least one [kind of] different nucleic acid fragment subjected to an additional modification, and the additional modification in one [kind of] different said nucleic acid fragment is [introduction of] a marker or a moiety [capable of binding] bound to a solid-phase carrier, [into] wherein said marker or moiety is additionally bound to a 5'-terminal side of the nucleic acid fragment.

13. (Twice Amended) The primer according to claim 8, wherein said primer comprises at least one kind of nucleic acid fragment subjected to an additional modification, and the additional modification in one kind of said nucleic acid fragment is [introduction of] a marker or a moiety [capable of binding] bound to a solid-phase carrier, wherein said marker or moiety is additionally bound to [into] a 5'-terminal side of the nucleic acid fragment.

14. (Twice Amended) The primer according to claim 5, wherein [a] the marker or [a] the moiety [capable of binding] bound to a solid-phase carrier [to be introduced into a molecule as an additional modification] is [any of] a biotin residue, a 2,4-dinitrophenyl group, [and] or a digoxigenin residue.

15. (Twice Amended) The primer according to claim 6, wherein [a] the marker or [a] the moiety [capable of binding] bound to a solid-phase carrier [to be introduced into a molecule as an additional modification] is [any of] a biotin residue, a 2,4-dinitrophenyl group, [and] or a digoxigenin residue.

16. (Twice Amended) The primer according to claim 7, wherein [a] the marker or [a] the moiety [capable of binding] bound to a solid-phase carrier [to be introduced into a molecule as an additional modification] is [any of] a biotin residue, a 2,4-dinitrophenyl group, [and] or a digoxigenin residue.

17. (Twice Amended) The primer according to claim 9, wherein [a] the marker or [a] the moiety [capable of binding] bound to a solid-phase carrier [to be introduced into a molecule as an additional modification] is [any of] a biotin residue, a 2,4-dinitrophenyl group, [and] or a digoxigenin residue.

18. (Twice Amended) The primer according to claim 10, wherein [a] the marker or [a] the moiety [capable of binding] bound to a solid-phase carrier [to be introduced into a molecule as an additional modification] is [any of] a biotin residue, a 2,4-dinitrophenyl group, [and] or a digoxigenin residue.--

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